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PTO/SB/21 (08-03)

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**TRANSMITTAL  
FORM**

(to be used for all correspondence after initial filing)

Application Number	10/717,244
Filing Date	November 19, 2003
First Named Inventor	Sharma
Art Unit	1641
Examiner Name	Not Yet Assigned
Attorney Docket Number	01130.US1

Total Number of Pages in This Submission

**ENCLOSURES (Check all that apply)**

- |   |  |  |
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| <input checked="" type="checkbox"/> Fee Transmittal Form<br><input type="checkbox"/> Fee Attached<br><input type="checkbox"/> Amendment/Reply<br><input type="checkbox"/> After Final<br><input type="checkbox"/> Affidavits/declaration(s)<br><input type="checkbox"/> Extension of Time Request<br><input type="checkbox"/> Express Abandonment Request<br><input checked="" type="checkbox"/> Information Disclosure Statement<br><input type="checkbox"/> Certified Copy of Priority Document(s)<br><input type="checkbox"/> Response to Missing Parts/Incomplete Application<br><input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s)<br><input type="checkbox"/> Licensing-related Papers<br><input type="checkbox"/> Petition<br><input type="checkbox"/> Petition to Convert to a Provisional Application<br><input type="checkbox"/> Power of Attorney, Revocation<br><input type="checkbox"/> Change of Correspondence Address<br><input type="checkbox"/> Terminal Disclaimer<br><input type="checkbox"/> Request for Refund<br><input type="checkbox"/> CD, Number of CD(s) _____ | <input type="checkbox"/> After Allowance communication to Group<br><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences<br><input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)<br><input type="checkbox"/> Proprietary Information<br><input type="checkbox"/> Status Letter<br><input type="checkbox"/> Other Enclosure(s) (please identify below): |
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Remarks

**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT**

Firm or Individual name	Pharmacia & Upjohn Company	Edward F. Rehberg 34,703
Signature	<i>Edward F. Rehberg</i>	
Date	June 8, 2004	

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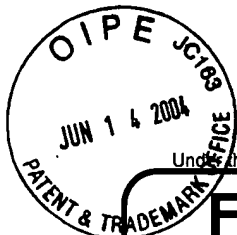
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PTO/SB/17 (10-03)  
Approved for use through 07/31/2006. OMB 0651-0032  
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# FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$)**180.00**

## Complete if Known

Application Number	10/717,244
Filing Date	November 19, 2003
First Named Inventor	Sharma
Examiner Name	Not Yet Assigned
Art Unit	1641
Attorney Docket No.	01130.US1

## METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit  
Account  
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21-0718

Pharmacia & Upjohn Company

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☐ Charge any additional fee(s) or any underpayment of fee(s)

☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

## FEE CALCULATION

### 1. BASIC FILING FEE

Large Entity		Small Entity		Fee Description	Fee Paid
Fee Code	Fee (\$)	Fee Code	Fee (\$)		
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	
SUBTOTAL (1)					(\$) <b>0.00</b>

### 2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims	Fee from below	Fee Paid
Total Claims		-20** = 0	X \$0.00	= \$0.00
Independent Claims		-3** = 0	X \$0.00	= \$0.00
Multiple Dependent			\$0.00	= \$0.00

Large Entity		Small Entity		Fee Description
Fee Code	Fee (\$)	Fee Code	Fee (\$)	
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$)**0.00**

\*\*or number previously paid, if greater; For Reissues, see above

## FEE CALCULATION (continued)

### 3. ADDITIONAL FEES

Large Entity Small Entity

Fee Code	Fee (\$)	Fee Code	Fee (\$)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for ex parte reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	180.00
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) \_\_\_\_\_

\*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$)**180.00**

## SUBMITTED BY

Name (Print/Type)	Edward F. Rehberg	Registration No. (Attorney/Agent)	34,703	Telephone	(269) 833-7829
Signature	<i>Edward F. Rehberg</i>	Date	June 8, 2004		

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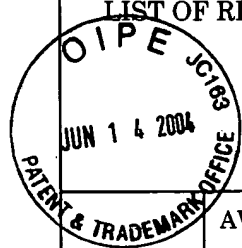
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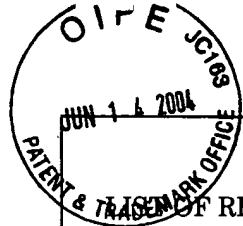
<b>LIST OF REFERENCES CITED BY APPLICANT</b> <i>(Use several sheets if necessary)</i>				Atty. Docket No. 01130.US1		Serial No. 10/717,244	
				Applicant      SK Sharma			
				Filing Date    November 19, 2003		1641	

OIPE  
 JUN 14 2004  
 PATENT & TRADEMARK OFFICE

U.S. PATENT DOCUMENTS								
Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate	
	AA	6,448,229	Sept. 10, 2002	Teall	514	19		
	AB	5,877,399	Mar. 2, 1999	Hsiao et al.	800	2		
	AC	5,811,633	Sept. 22, 1998	Wadsworth et al.	800	2		
	AD	5,387,742	Feb. 7, 1995	Cordell	800	2		
	AE	4,431,546	Feb. 14, 1984	Hughes et al.	210	656		
	AF	4,227,437	Oct. 14, 1980	Inloes et al.	84	454		
	AG	3,996,345	Dec. 7, 1976	Ullman et al.	424	12		
	AH	3,939,350	Feb. 17, 1976	Kronick et al.	250	365		
	AI	3,850,752	Nov. 26, 1974	Schuurs et al.	195	103.5 R		
	AJ	3,817,837	June 18, 1974	Rubenstein et al	195	103.5 R		
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		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	AK	WO 91/18982	Dec. 12, 1991	WIPO	C12N	15/12		
	AL	WO 01/83811	Nov. 8, 2001	WIPO	C12Q	1/00		
	AM	WO 01/62897	Aug. 30, 2001	WIPO	C12N	5/06		
	AN	EP A 0367566	Oct. 31, 1989	WIPO	C12N	15/12		
OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)								
	AO	Barany and Merrifield, The Peptides, Gross and Meienhofer, eds. Academic Press, New York, 1-284, (1979)						
	AP	Berezovska, et al., J. Biol. Chem., <i>Notch1 and Amyloid Precursor Protein Are Competitive Substrates for Presenilin1-dependent <math>\gamma</math>-Secretase Cleavage</i> , 276:30018-30023, (2001)						
	AQ	Better, et al., Science, 240:1041-43, (1988)						
	AR	Bittner, et al., Methods in Enzymol. 153:516-544, (1987)						
	AS	Cane, David E., et al., Science, <i>Harnessing the Biosynthetic Code: Combinations, Permutations, and Mutations</i> , 282:63-68, (October 1, 1998)						
	AT	Capaldi, et al., Biochem. Biophys. Res. Comm., 76:425-433, (1977)						
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		Applicant SK Sharma	
		Filing Date November 19, 2003	1641
AW	Davis, et al., Biotechnol Bioeng., <i>New Fusion Protein Systems Designed to Give Soluble Expression in Escherichia coli</i> , 65(4):382-388, (November 20, 1999)		
AX	De Stropper, et al., Nature, <i>A presenilin-1-dependent <math>\gamma</math>secretase-like protease mediates release of Notch intracellular domain</i> , 398:518-522, (1999)		
AY	Dovey, et al., J. Neurochem., <i>Functional gamma-secretase inhibitors reduce beta-amyloid peptide levels in brain</i> , 76:173-181, (2001)		
AZ	Engelhard E. K., et al., Proc. Nat. Acad. Sci., <i>The insect tracheal system: A conduit for the systemic spread of Autographa californica M nuclear polyhedrosis virus</i> , 91:3224-3227, (1994)		
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BD	Houston and Banks, Curr. Opin. Biotechnol., <i>The chemical-biological interface; developments in automated and miniaturized screening technology</i> , 8:734-740, (1997)		
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BF	Kang, et al., Nature, <i>The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor</i> , 325:733-736 (February 19, 1987)		
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BL	Macejak and Sarnow, Nature, <i>Internal initiation of translation mediated by the 5' leader of a cellular mRNA</i> , 353:90-94, (September 5, 1991)		
BM	Marambaud et al., EMBO J., <i>A presenilin-1/ <math>\gamma</math>secretase cleavage releases the E-cadherin intracellular domain and regulates disassembly of adherens junctions</i> , 21(8):1948-1956, (2002)		
BN	Merrifield, Bruce; Science, <i>Solid Phase Synthesis</i> , 232:341-347, (April 18, 1986)		
BO	Myers, Peter L., Curr. Opin. Biotechnol., <i>Will combinatorial chemistry deliver real medicines?</i> , 8:701-707, (1997)		
BP	Okayama and Berg, Mol. Cell. Biol., <i>A cDNA Cloning Vector That Permits Expression of cDNA Inserts in Mammalian Cells</i> , 3(2):280-289, (February 1983)		



<b>REFERENCES CITED BY APPLICANT</b> <i>(Use several sheets if necessary)</i>		Atty. Docket No. 01130.US1	Serial No. 10/717,244
		Applicant SK Sharma	
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	BQ	Okochi et al., EMBO J., <i>Presenilins mediate a dual intramembranous <math>\gamma</math>-secretase cleavage of Notch-1</i> , 21(20), 5408-5416, (2002)	
	BR	R. E. Olson, et al., Curr. Opin. Drug Discovery & Develop., Progress Towards Testing the Amyloid Hypothesis: Inhibitors of APP Processing, 4(4):390-401, (July 2001) XP008028676	
	BS	Pelletier and Sonenberg, <i>Nature</i> , Internal initiation of translation of eukaryotic mRNA directed by a sequence derived from poliovirus RNA, 334:320-325, (July 28, 1988)	
	BT	Petit A., et al., "New Protease Inhibitors prevent GammaSecretase-Mediated Production of Abeta40/42 Without Affecting Notch Cleavage", Nature Cell Biology, MacMillan Publishers, GB 3(5), May 2001, 507-511 XP001015215	
	BU	P. Ponte et al., A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors, <i>Nature</i> , 331(11):525-527 (February 11, 1988)	
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	BX	D Scharf et al., Results Probl Cell Differ 20:125-62, (1994)	
	BY	Eric H. Schroeter et al., <i>Nature</i> , Notch-1 signalling requires ligand-induced proteolytic release of intracellular domain, 393:382-386, (May 28, 1998)	
	BZ	Smith, Gale E., et al., J. Virol., <i>Molecular Engineering of the Autographa californica Nuclear Polyhedrosis Virus Genome: Deletion Mutations Within the Polyhedrin Gene</i> , 46(2):584-593, (May 1983)	
	CA	Stewart and Young, Solid Phase Peptide Synthesis, 2 <sup>nd</sup> ed., Pierce Chemical Co., Chapter 3, p 125-135, (1984)	
	CB	Tam, James P., et al., J. Am. Chem. Soc., S <sub>N</sub> 2 Deprotection of Synthetic Peptides with a Low Concentration of HF in Dimethyl Sulfide: Evidence and Application in Peptide Synthesis <sup>1</sup> , 105(21):6442-6455, (1983)	
	CC	Tanzi, et al., <i>Nature</i> , 331: 528-530, (1988)	
	CD	Wilkinson and Haass, Bio/Technology 9, 443-448, (May 1991)	
	CE	Michael S. Wolfe and Christian Haass, J. Biol. Chem., The Role of Presenilins in $\gamma$ -Secretase Activity, 276(8):5413-5416, (February 23, 2001)	
	CF	Younkin, Steven G., <i>Brain Pathol.</i> , Processing of the Alzheimer's disease $\beta$ A4 Amyloid Protein Precursor (APP), 1(4):253-62, 1991	
Examiner		Date Considered	